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Enterococcus-associated urinary tract infections, their prevalence and antibiotic resistance

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Abstract

Background:
Methodology: A retrospective study was conducted using the Medical Microbiology Laboratory records of the Lagos State University Teaching Hospital. The study reviewed the in vitro antibiotic susceptibility patterns of urinary bacterial isolates from April 2020 to March 2021, focusing on Enterococcus spp. Bacteria were isolated and identified from routine urine samples using standard bacteriological methods and the Analytical Profile Index (API). Antibiotic susceptibility tests (AST) were performed using the modified Kirby-Bauer disk diffusion method, with susceptibility breakpoints determined by the Clinical and Laboratory Standards Institute (CLSI) guidelines.
Results: A total of 82 patients (5 outpatients and 77 inpatients) with *Enterococcus*-associated UTIs were identified. The species distribution was 70.7% *E. faecalis* and 29.3% *E. faecium. E. faecium* exhibited greater resistance to levofloxacin and tetracycline but greater sensitivity to amoxicillin compared to *E. faecalis*. Both species showed high sensitivity to tigecycline, meropenem, and fosfomycin.
Conclusion: The prevalence of Enterococcus-associated UTIs in this study was 3.6% (82/2253), with hospital-acquired *Enterococcus* spp. accounting for 3.4% (77/2253). *E. faecium* isolates were significantly more resistant to levofloxacin and tetracycline than *E. faecalis*. The high rate of multidrug resistance (MDR) in both species underscores the importance of promoting rational antibiotic use to prevent the emergence of resistant organisms.

Keywords; *Enterococcus species*, Uropathogens, UTI, MDR

Introduction

In addition to colonizing the mouth cavity, genitourinary tract, and skin, particularly in the perineal region of healthy individuals, *Enterococcus* spp. make up the typical intestinal flora of humans and animals. Typically, colonization rather than infection is indicated when enterococci are isolated from clinical specimens. However, enterococcal organisms can also result in infections; the most common infection is a UTI, which is followed by septicemia, endocarditis, meningitis, and wound infections.[1]

While there are over 49 species in the genus *Enterococcus,* only a small number of them can lead to serious infections in humans.[2] More than 90% of human infections are caused by *E. faecalis* and *E. faecium*, which are the most common species.[3] Due to their intrinsic and acquired resistance to a variety of antibiotics, *Enterococcus* spp. pose a significant treatment problem. Only a few medications remain

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effective, including nitrofurantoin, linezolid, and quinupristin-dalfopristin, because of the emergence of vancomycin-resistant *Enterococcus* (VRE). The prevalence of VRE ranges from 1% to 30% in Europe and 20% to 30% in the United Kingdom.[4] Other *Enterococcus* spp. known to cause human infections include *E. avium, E. gallinarum, E. casseliflavus, E. durans, E. raffinosus,* and *E. mundtii*. Of the enterococci species known to cause human infections, 85–90% are caused by E. faecalis, and 5–10% by *E. faecium*.[5,6,7]

The urinary tract, wounds, and biliary tract are the most prevalent locations for *enterococci* infections in patients, often alongside other bacterial species, making it challenging to determine the pathogenic role of *enterococci*.[8] According to Gordon et al.[6], *enterococcal* infections are equally distributed between the sexes. However, because urine catheterization is more common in older patients and in healthy women than in men, urinary tract infections are more common in these populations.

Enterococcus spp. contribute to over 30% of nosocomial UTIs and have been identified as the second leading pathogen in catheter-associated UTIs (CAUTI).[9,10] They are identified in routine microbiology laboratories by their morphological appearance on Gram stain and culture. They can be differentiated from non-group D streptococci by their ability to grow in 6.5% NaCl, hydrolyze aesculin, survive in the presence of 40% bile, and show positive results on the pyrrolidonyl arylamidase test.[2] The management of *enterococcal* infections is typically challenging due to their resistance to aminoglycosides and β-lactam antibiotics; however, a combination of these medications may work well together. Vancomycin, a glycopeptide, was the preferred medication; nevertheless, drug resistance is currently rising. Vancomycin-resistant *enterococci* infections are currently treated with more recent antibiotics, such as quinupristin and dalfopristin combined.[11]

A study carried out in Osogbo, Nigeria,[12] placed the prevalence of hospital-acquired *Enterococcus* at 5.9%. However, the prevalence and magnitude of *Enterococci*-associated UTIs in this environment are largely unknown. In Nigeria, the role of enterococci in clinical infections has not been fully appreciated, hence reports of *enterococcal* infections are very few. The objectives of this study are to determine the prevalence of *Enterococcus*-associated UTIs, identify the common species in our health facility, and determine their susceptibility profile to commonly prescribed antibiotics. This information will serve as pilot data for more extensive molecular epidemiology of *enterococcal* infections, which will be necessary for the formulation of control policies in this environment.

Materials and Methods

Study setting

The study was conducted in the Department of Medical Microbiology at Lagos State University Teaching Hospital, an 800-bedded tertiary center located in Ikeja, Lagos, southwest Nigeria. The hospital is dedicated to teaching, research, and specialist services, serving Lagos State and neighboring states in southwest Nigeria.

Study Design

This retrospective study involved a review of the Medical Microbiology Laboratory records to analyze the antimicrobial susceptibility profiles of Gram-positive cocci bacterial urinary isolates, especially *Enterococcus* spp., obtained between April 2020 and March 2021. Patients' case notes were retrieved to extract relevant clinical history of possible risk factors.

Isolation and Antibiotic Susceptibility Pattern of Bacterial Isolates

Normal processing of urinary samples in the laboratory during the review period involved macroscopic and microscopic examination. Urinary samples were inoculated into Cystine Lactose Electrolyte Deficient (CLED) and Blood agar plates and incubated aerobically at 35-37°C for 18-24 hours. Isolates were identified using conventional biochemical tests and the Analytical Profile Index (API). Antimicrobial susceptibility testing (AST) was performed using the modified Kirby-Bauer disk diffusion method. Susceptibility breakpoints were determined using Clinical and Laboratory Standards Institute (CLSI) guidelines.[13]

Data Analysis

Data analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 22. The analysis included descriptive statistics to summarize patient demographics, species distribution, and antimicrobial susceptibility patterns. Frequency distributions and percentages were used to describe categorical variables, while means and standard deviations were used for continuous variables. Comparative analyses were conducted to evaluate the differences in susceptibility patterns between *E. faecalis* and *E. faecium* isolates.

Ethical considerations

Ethical approval for the study was obtained from Lagos State University Teaching Hospital Research and Ethics Committee. As data were retrospectively obtained from the laboratory records and patients' case notes, informed consent was not deemed necessary. However, privacy and confidentiality of patients' data were protected.

Results

A total of 2,253 urine samples were processed in the medical microbiology laboratory over the one-year study period. Among these, 662 (29.4%) yielded positive cultures, with 164 (24.8%) identified as Gram-positive cocci isolates. Among the Gram-positive cocci isolates, 82 patients (5 outpatients and 77 inpatients) were identified with *Enterococcus*-associated UTIs. The majority of these *Enterococcus* spp. isolates were from male patients (53.4%). The species distribution showed 70.7% *E. faecalis* and 29.3% *E. faecium*.

Table 1: Distribution of urine samples and isolates

Category	Frequency	Percentage (%)
Total urine samples	2,253	100
Positive cultures	662	29.4
Gram-positive cocci	164	24.8
Gram-positive bacilli	4	0.6
Gram-negative bacilli	494	74.6

Table 2: Distribution of *Enterococcus* spp. by species and patient demographics

Category	Frequency	Percentage (%)
E. faecium	24	14.6
E. faecalis	58	35.4
Other Gram-positive cocci	82	50.0
Total	164	100
Male	43	53.4
Female	39	46.6
Outpatient	5	6.1
Inpatient	77	93.9

TABLE 3: Antibiotic susceptibility patterns of *enterococcus* species

Organisms	Antibiotics	Sensitivity	Intermediate	Resistance	Total
Enterococcus Faecium	Cefotaxime	10(41.7%)	2(8.3%)	12 (50%)	24
	Amoxicillin–Clavulanate	14(58.3%)	——	10 (41.7%)	
	Levofloxacin	10(41.7%)	2(8.3%)	12 (50%)	
	Tigecycline	17(70.8%)	2(8.3%)	5 (20.8%)	
	Amoxicillin	20(83.3%)	3(12.5%)	1 (4.3%)	
	Fosfomycin	17(70.8%)	5(20.8%)	2 (8.3%)	
	Streptomycin	10(41.7%)	——	14 (58.3)	
	Tetracycline	14(58.3%)	4(16.7%)	6 (25%)	
	Meropenem	21(87.5%)	2(8.3%)	1 (4.2%)	
	Gentamycin	5(20.8%)	2(8.3%)	17(70.8%)	
Enterococcus Faecalis	Amoxicillin-Clavulanate	20(34.5%)	16(33.3%)	22(37.9%)	58
	Amoxicillin	28(48.3%)	——	30(51.7%)	
	Cefotaxine	15(25.9%)	10(20.8%)	33(56.9%)	
	Tigercycline	46(79.3%)	12(20.7%)	——	
	Fosfomycin	58(100%)	——	——	
	Meropenem	54(93.1%)	2(3.4%)	2(3.4%)	
	Erythromycin	30(51.7%)	6(10.3%)	22(37.9%)	
	Levofloxacin	38(65.5%)	2(3.5%)	18(31.0%)	
	Tetracycline	40(83.3%)	18(16.7%)	——	
	Streptomycin	20(34.5%)	8(13.8%)	30(51.7%)	
	Gentamycin	10(20.8%)	8(13.8%)	40(83.3%)	

Antibiotic susceptibility testing revealed that most *E. faecalis* and *E. faecium* isolates were sensitive to fosfomycin (70%-100%), tigecycline (70%-79.3%), and meropenem (86%-93.1%). However, high-level gentamicin resistance was observed in these isolates. Additionally, these *Enterococcus* species exhibited significant resistance to streptomycin (51%-58.3%), cefotaxime (50%-56.9%), and amoxicillin-clavulanate (36%-41.7%). *E. faecium* showed greater resistance to quinolones and tetracyclines but greater sensitivity to amoxicillin compared to *E. faecalis*.

Discussion

In this study, 82 patients (5 outpatients and 77 inpatients) were identified with *Enterococcus*-associated UTIs. The prevalence of *Enterococcus*-associated UTIs was 3.6%, with hospital-acquired *Enterococcus* spp. accounting for 3.4% of cases. This prevalence is comparable to a study conducted in Oshogbo, Nigeria, which reported a 5.9% prevalence of hospital-acquired *Enterococcus* infections.[12]

Enterococcus spp. are known to survive for extended periods on various surfaces, including highly cleaned hospital environments, making them common in hospital settings.[14] Among the patients, 43 (53.4%) were male, and 39 (46.6%) were female. There are several hypotheses explaining why men may be more susceptible to *Enterococcus* infections. One hypothesis suggests that the prostate gland in men can harbor bacteria, leading to the development of micro-abscesses. Bacteria can migrate from the digestive system to the prostate tissue, which has been associated with prostate cancer and detected in sperm.[15,16] Another factor is the presence of prostate stones, which can develop secondary infections, forming biofilms on the stones and within the prostate. Urological research indicates that detecting and treating prostate stones can reduce recurrent infections.[17]

Most isolates of *Enterococcus faecalis* and *Enterococcus faecium* were sensitive to fosfomycin (70%-100%), tigecycline (70%-79.3%), and meropenem (86%-93.1%). These results are consistent with other studies showing fosfomycin's efficacy against *Enterococcus,* including vancomycin-resistant strains (VRE).[18,19] Fosfomycin is approved for treating uncomplicated UTIs as a single 3g oral dose, achieving high urine concentrations and being well tolerated.[20,21]

High-level resistance to gentamicin and streptomycin was observed in these isolates, similar to findings in other studies.[22] Notably, *E. faecium* showed greater sensitivity to amoxicillin compared to *E. faecalis*, contrasting with a Nigerian study that reported 100% susceptibility of *E. faecalis* to amoxicillin.[22]

These findings highlight the importance of continuous monitoring and rational antibiotic use to manage and prevent the emergence of resistant *Enterococcus* strains in clinical settings.

Conclusion

The study provides more information of the prevalence and antimicrobial susceptibility patterns of *Enterococcus*-associated urinary tract infections (UTIs) in a tertiary hospital in Lagos, Nigeria. Over the one-year study period, 3.6% of UTIs were associated with *Enterococcus* species, with hospital-acquired cases accounting for 3.4%. The distribution of Enterococcus spp. showed a higher prevalence of *E. faecalis* (70.7%) compared to *E. faecium* (29.3%). Male patients constituted a slightly higher proportion of cases (53.4%), which may be attributed to specific urological factors such as prostate conditions that can harbor bacteria and lead to recurrent infections. Antibiotic susceptibility testing revealed that most isolates were highly sensitive to fosfomycin, tigecycline, and meropenem. However, high-level resistance to gentamicin and streptomycin was observed, highlighting the need for careful selection of antibiotics. Further research into the molecular epidemiology of *Enterococcus* infections is necessary to inform and improve infection control policies in healthcare settings.

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